REMARKS

Claims 4-5, 9-10, and 14-18 have been canceled without prejudice to continued prosecution. Claim 1 has been amended to recite that the sequence variant is at a position selected from the group consisting of nucleotide 230 of SEQ ID NO:5, nucleotide 559 of SEQ ID NO:5, nucleotide 642 of SEQ ID NO:3, and nucleotide 1037 of SEQ ID NO:5. Support for this amendment can be found, for example, at page 16, Table 4. Claims 6-8 and 11-13 have been amended for clarity. New claim 19 recites that the nucleotide 642 variant is a substitution of a guanine for a cytosine. Support for claim 19 can be found, for example, in Table 4 on page 16 and the sequence of Figure 3. No new matter has been added.

The specification has been amended to incorporate sequence identifiers. Table 4 of the specification also has been amended to indicate that the intron 6 polymorphism at position 642 of Figure 3 (SEQ ID NO:3) is a change from a "C" to a "G." The Table as originally filed indicated that it was a "G" to a "C" change. As indicated in Figure 3, however, position 642 in the reference sequence is a "C." Thus, it is clear that the variant refers to the substitution of a "G." No new matter has been added.

Applicants respectfully request reconsideration and allowance of claims 1-3, 6-8, 11-13, and 19 in view of the above amendments and following remarks.

Priority

The Examiner indicated that Applicant has not complied with all of the conditions for receiving the benefit of an earlier filing date under 35 U.S.C. §119(e). As indicated by the Examiner, the transmittal letter of April 5, 2001, which was filed with the present application, and the Declaration filed on December 14, 2002, each claimed priority to provisional application 60/195,665, filed April 7, 2000. Applicants have amended the specification to contain a specific reference to the provisional application. As the initial priority claim was made within four months from the actual filing date of the application, it is not believed that a petition is necessary.

Information Disclosure Statement

The Examiner included additional identifying information for three of the references on the Form-1449 submitted with the Information Disclosure Statement submitted June 27, 2001. The information added to the Form-1449 is accurate.

Sequence Identifiers

The Examiner indicated that the specification and drawings did not contain appropriate sequence identifiers. Applicants have added sequence identifiers throughout the application, including to the description of the drawings. Thus, the application is in compliance with the requirements of 37 C.F.R. §1.821-1.825.

Specification

The Examiner objected to the specification for containing an embedded hyperlink. Applicants have amended the specification at page 2 to refer to the worldwide web at ncbi.nlm.nih.gov/omim.

The Examiner noted the use of the trademarks QIAamp®, Wizard®, and A.S.A.P.™ in the application and requested that the trademarks be capitalized wherever they appear and be accompanied by generic terminology.

The proper trademark symbol follows each trademark. In addition, the specification refers to each of these trademarks as kits for extracting genomic DNA. See page 7, 2nd full paragraph, of the specification. The Examiner is requested to withdraw the objections to the specification.

Rejections under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 6-7, 9-10 and 12 under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Examiner asserted that it was unpredictable whether one of skill in the art could make and use the claimed nucleic acids. The Examiner also alleged that the specification does not provide any evidence that the C230G, C559T, and G642C polymorphisms are associated with diabetes, obesity, or any other metabolic disorder. The Examiner further alleged that the claims "encompass nucleic acid molecules comprising such PRKAG3 sequences (i.e., molecules in which sequences flanking the "PRKAG3 sequence" have no relationship to

PRKAG3)" and that the claims "do not include any sort of functional requirement for the claimed nucleic acids."

Applicants have canceled claims 9-10 without prejudice to continued prosecution. The specification provides sufficient guidance for one of skill in the art to make and use the claimed nucleic acids of claims 6-7 and 12. As indicated in the specification at page 5, first paragraph, nucleic acid molecules can be produced by standard techniques. The sequence of human PRKAG3 is publicly available in GenBank under Accession No. AC009974. See, Example 1, page 12 of the specification. Specific point changes can be introduced into wild-type sequence using oligonucleotide-directed mutagenesis, polymerase chain reaction (PCR) techniques, or chemical synthesis. See, for example, the specification at page 5, last paragraph, through page 6, third paragraph.

Nucleic acids containing sequence variants at each of the recited positions can be used as probes and primers. See, specification at page 5, 2nd paragraph. For example, as indicated at page 7 of the specification, such nucleic acid molecules can be specifically hybridized to a PCR product to determine if the product contains the variant nucleic acid sequence. Such nucleic acid molecules also can be used to develop primers that can be used to amplify a product only when the variant allele is present (MSPCR or allele-specific PCR). See, for example, pages 8-9 of the specification. Thus, in view of the guidance in the specification, one of ordinary skill in the can make and use the claimed nucleic acids.

The Examiner rejected claims 1-5, 8 and 11 under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Examiner asserted that the specification does not provide enablement for isolated nucleic acid molecules "comprising a human PRKAG3 sequence" that comprise any "nucleotide sequence variant," as set for the in the instant claims.

Applicants have amended claim 1 to recite that the isolated nucleic acid includes a nucleotide sequence variant at a position selected from the group consisting of nucleotides 230, 559, 642, and 1037. As discussed above, the specification enables one of ordinary skill in the art and to make and use the claimed nucleic acid molecules. In particular, the specification provides guidance on how to make nucleic acid molecules that include a sequence variant. See, for example, the specification at page 5, last paragraph, through page 6, third paragraph. The specification also provides guidance on using such nucleic acid molecules for probes and

primers. See, specification at page 5, 2nd paragraph, and pages 7-9 of the specification. Thus, one of ordinary skill in the art can make and use the claimed nucleic acid molecules. The Examiner is requested to withdraw the rejections under 35 U.S.C. §112, first paragraph.

Rejections under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 6-8 and 11-13 under 35 U.S.C. § 112, second paragraph, as being indefinite. The Examiner asserted that the phrase "said exon variant" lacked antecedent basis in claims 6-8. This phrase is not recited in amended claims 6-8.

The Examiner asserted that claims 6-8 were indefinite in that it was "unclear as to whether the numbers 230, 550, and 1037 are intended to refer to the location of substations in the claimed "isolated nucleic acid molecules," in a particular SEQ ID NO, in the recited exon (e.g., exon 3, exon 4, or exon 10) in the PRGAG3 genomic sequence or coding sequence, etc." Claim 1, from which claims 6-8 depend, has been amended to recite the particular sequence identifier for each nucleotide sequence variant.

The Examiner asserted that the phrase "said PRKAG3 nucleic acid sequence" in claim 11 lacked sufficient antecedent basis. Applicants have amended claim 11 as suggested by the Examiner.

The Examiner alleged claims 12-13 to be indefinite in that it was:

> unclear as to whether the claims are intended to be limited to nucleic acid molecules in which the PRKAG3 sequence encodes variations of the particular amino acids of the PRKAG3 polypeptide disclosed in the specification (i.e., in which codons 71/340 of the PRKAG3 coding sequence are altered), or whether the claims are intended to also encompass, e.g., nucleic acids encoding PRKAG3 polypeptides, wherein those polypeptides further comprise any type of "amino acid sequence variant" molecule that includes the substitutions recited in claims 12-13.

Claims 12-13 have been amended to include the sequence identifier for the polypeptide. Thus, it is clear that claims 12-13 encompass polypeptides that include a variant at positions 71 and 340, respectively, of SEQ ID NO:6.

Applicants submit that claims 6-8 and 11-13 are sufficiently definite. The Examiner is requested to withdraw the rejections under 35 U.S.C. §112, second paragraph.

Rejections under 35 U.S.C. § 102

The Examiner rejected claims 1 and 4-5 under 35 U.S.C. § 102(b) as being clearly anticipated by Cheung et al. (Biochem. J., 2000, 346(Pt. 3):659-669). The Cheung et al. reference was characterized as disclosing a coding sequence for the γ3 subunit of human AMP-activated protein kinase that contains sequence variants with respect to the coding sequence disclosed by Applicant.

Claims 4-5 have been canceled without prejudice to continued prosecution. Claim 1 has been amended to recite that the isolated nucleic acid includes a nucleotide sequence variant at a position selected from the group consisting of nucleotide 230 of SEQ ID NO:5, nucleotide 559 of SEQ ID NO:5, nucleotide 642 of SEQ ID NO:3, and nucleotide 1037 of SEQ ID NO:5. The Cheung et al. reference does not disclose a sequence variant at the recited positions. Thus, the Cheung et al. reference does not anticipate claim 1. The Examiner is requested to withdraw the rejection of claim 1 under 35 U.S.C. §102(b).